

Treatment Human Breast Cancer Stem Cells with Exosomes Bearing LNA-antimicroRNA-3-142p Can Decrease their Tumorigenicity

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Abstract

Introduction Exosomes, widely recognized natural nanovesicles, represent one of the recently discovered modes of intercellular communication with their ability to transmitting crucial cellular information (e.g., mRNA, microRNAs and proteins) from parent cell to numerous distant recipient cells. Exosomes are widely distributed in body fluids and involved in multiple diseases processes and can be engineered to have robust delivery and targeting capacity. Breast cancer stem cells (BCSCs) have been suggested as the roots of chemo- and radio-therapy resistance. It's reported that miR-142 is upregulated in human breast cancer stem cells as compared to the non-tumorigenic breast cancer cells. In this study, we report that mesenchymal stem cells derived-exosomes can efficiently deliver anti-miR-142 into the MCF-7 derived-BCSCs to decrease clonogenicity and tumorigenicity of BCSCs.

Materials and Methods: Bone marrow derived-MSCs were characterized. Exosomes were isolated from cultured MSCs using exospin kit and characterized using Western blotting and transmission electron microscopy. BCSCs derived from MCF-7 by culturing in low attachment plate and then identified by immunophenotyping. Exosomes were loaded by anti-miR-142 molecules using electroporation, cocultured with BCSCs to delivery anti-miR-142 molecules. MicroRNA-142 and APC gene levels were measured by real time PCR.

Results: Exosomes loading efficiency was analyzed by fluorimetry that was approximately 60%. BCSCs appeared as tumorspheres in low attachment plate after 7 days. Exosomes bearing antimicroRNA-142 were observed inside the cells by 3D fluorescent microscopy. Expression of mir-142 and mir-150 decreased in BCSCs after treatment with the exosomes (P<0.05).

Conclusions: In this study, we showed that MSCs-derived exosomes could be used as a feasible nanovehicle to deliver drug molecules like anti-miR-142 into BCSCs only by coculturing. We observed that reducing the level of mir-142 in the BCSCs by using exosomes nanocarriers can reduce the growth of BCSCs.